# Optimizing photodynamic therapy regimens

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**Title:** Optimising PDT regimes: variables in irradiation may influence outcomes

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Topical photodynamic therapy (PDT) is widely accepted as an effective treatment for superficial basal cell carcinoma (sBCC). As with other non-surgical approaches, clearance and recurrence rates are higher following PDT than definitive surgical excision, with overall clearance at one year of approximately 76% being expected[1]. For many patients this is a very suitable treatment approach, particularly if lesions are large and/or multiple or the patient is not suitable for surgery because of co-morbidities. However, optimising PDT outcomes through exploration of variables in treatment parameters, such as drug and light delivery is a priority.

Kessels and colleagues, report on a randomised controlled trial in which topical aminolaevulinic acid (ALA) PDT using a fractionated irradiation regime with a 2-hour dark interval delivered on one day was compared with conventional methyl aminolevulinate (MAL) PDT given as two treatments one week apart for sBCC[2]. This research group has previously undertaken pre-clinical and clinical studies, indicating that high clearance rates can be achieved using this fractionated ALA PDT regime[3]. The two-fold irradiation process resulted in superior clearance rates of sBCC compared with a single continuous irradiation when followed up to 5 years after treatment[4], supporting previous pre-clinical study observations[4,5]. The hypothesis is that increased efficiency of PDT may be achieved due to optimising reoxygenation during the dark interval and through an enhanced immune response[4].

In the current study, whilst there was a suggestion of higher clearance rates of sBCC one year after the fractionated ALA PDT regime compared with the MAL PDT regime, this was a non-significant result possibly due to the sample size and power of the study. Indeed, the fractionated ALA PDT regime resulted in greater side effects, notably pain. The study arms had several variables of prodrugs, application time of prodrugs, light sources and irradiation regimes. Therefore, given also that the differences in efficacy were non-significant, it is difficult to draw firm conclusions regarding the actual impact of the fractionation of irradiation per sae.

The study was well undertaken in robust format and building on the authors track record from earlier studies, together indicates that a fractionated ALA PDT regime undertaken within the same day is an option for effective treatment of sBCC, although patients need to be advised of the risk of higher pain levels. It would be most interesting to compare ALA PDT with MAL PDT both with fractionated irradiation as the only variable in a larger sample size.

This is an important contribution to the literature as it highlights that there may be many ways to optimally deliver effective PDT. Clinic arrangements and patient preference regarding acceptance of risk of discomfort with treatment and whether it is preferred to have treatment all in one longer day or to return for a second treatment at one week are factors to take into account. Whilst effective, we cannot conclusively say that there is a conferred advantage of a fractionated regime for effective clearance of sBCC and it may be at the trade-off of increased side effects but having options regarding how to deliver effective PDT is key and this certainly warrants further study.

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